Message

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Sent: 10/20/2017 3:15:51 PM
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Subject: GM Mosquitoes Closer to Release in U.S.

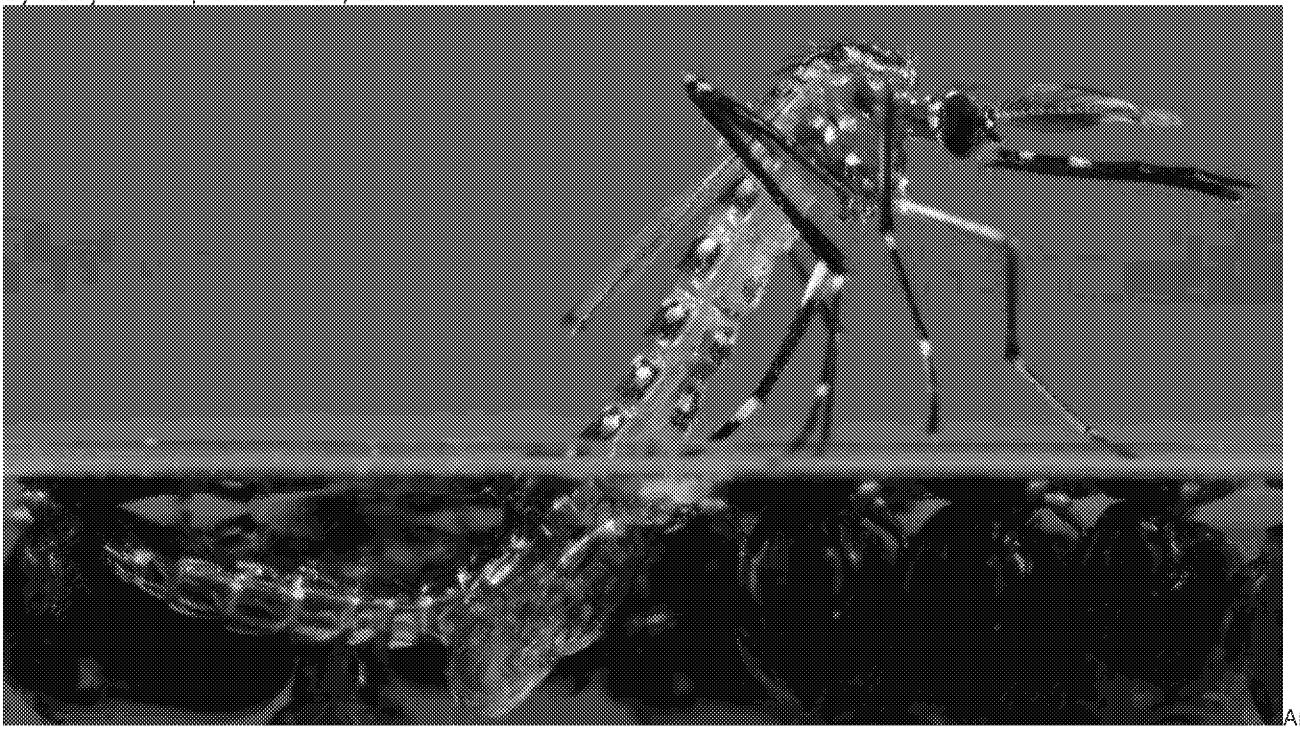
FYI

http://www.the-scientist.com/?articles.view/articleNo/50636/title/GM-Mosquitoes-Closer-to-Release-in-U-S-/

GM Mosquitoes Closer to Release in U.S.

The EPA is now in charge of regulating the use of Oxitec's strain of *Aedes aegypti*, genetically engineered to reduce populations of the insects.

By Abby Olena | October 13, 2017



An adult *Aedes aegypti* mosquito emerges from its pupal case.OXITEC

Last week (October 5), the United States Food and Drug Administration (FDA) announced that the US Environmental Protection Agency (EPA) will assume responsibility for overseeing the approval and use of mosquitoes genetically engineered to act as pesticides, specifically, a variety of *Aedes aegypti* generated by UK company Oxitec. This regulatory change could lead to pilot releases of the mosquitoes in the U.S. sometime in the next year.

"We hope within the next three to six months we will get regulatory permission to go ahead [with] releases of our mosquitoes in the U.S," says Derric Nimmo, a scientist at Oxitec.

"*Aedes aegypti* transmit dengue, Zika, and other viral diseases," explains North Carolina State University entomologist Fred Gould. Because vaccine development has thus far been challenging and the available dengue

vaccine is only partially effective, the current strategy for combatting these diseases is insect control, which includes spraying millions of dollars worth of insecticides. As an alternative, biotech firms have been working on developing tools like the genetically modified (GM) mosquitoes and mosquitoes infected with *Wolbachia,* a bacterium that can disrupt virus transmission from mosquito to human. "You need to come at it from all directions responsibly," Gould adds.

Nimmo says that Oxitec initially worked with the US Department of Agriculture, and then with the FDA in cooperation with experts from the EPA and the Centers for Disease Control and Prevention (CDC). In August 2016, an FDA assessment—prepared with input from EPA and CDC officials—suggested that deploying Oxitec's genetically modified (GM) mosquitoes would have no significant impact on the environment at a proposed release site in the Florida Keys.

It was a good sign for Oxitec, but residents balked at being a test site. And the FDA had yet to give approval for the insects' release. In the guidance issued last week, the FDA clarified that the Oxitec mosquitoes are not drugs because their use is not intended to cure or treat disease, but to limit mosquito populations, thereby functioning as a pesticide.

The switch from FDA to EPA oversight reflects the EPA's role in approval of pesticides, including traditional chemical pesticides used for mosquito control and others okayed by the agency that include GM microbial components. The EPA has also approved experimental release of *Wolbachia*-infected *A. aegypti* in Fresno County and Orange County, California, as well as in Monroe County, Florida, the location of the Florida Keys.

Mayor Gabriel Ferrato releases male Oxitec mosquitos from a van in Piracicaba, Brazil.OXITEC

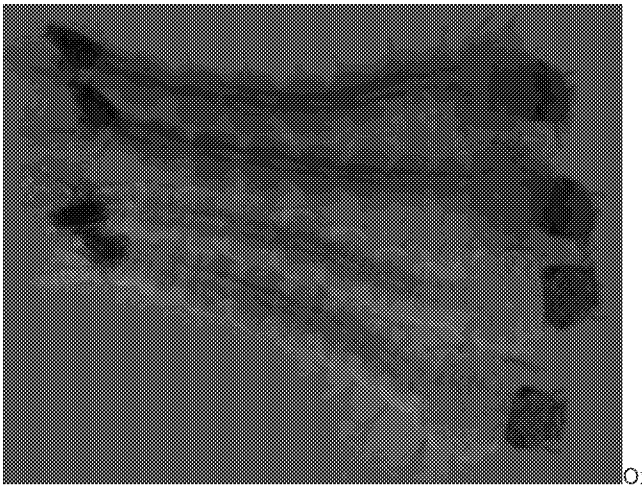
"EPA will regulate [genetically engineered] mosquitoes in the same way the agency regulates other pesticides," an EPA spokesperson writes in an email to *The Scientist.* "The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) gives EPA the authority to regulate the distribution, sale, and use of pesticide products to ensure they do not cause unreasonable adverse effects on people or the environment."

Approval times vary depending on the type of application, according to the EPA spokesperson. "At this point, EPA has not received an application from Oxitec," says the spokesperson, but typically, organizations begin by applying for an experimental use permit, at which point the agency has seven months to reach a decision. After collecting data in field testing, the organization can then apply for registration under FIFRA, and then the EPA has 13 to 25 months to complete its review.

Because experts from the EPA have collaborated with the FDA throughout Oxitec's application process—including on the August 2016 finding that the environmental impacts of releasing the mosquitoes would be minimal—Nimmo is optimistic that the EPA's regulatory process could move quickly.

"See After Harvey, Mosquito Control Ramps Up"

Oxitec researchers have engineered their mosquitoes with both a fluorescent reporter gene and a self-limiting gene that kills the insects at a young age, before they can reproduce. They breed adults by adding tetracycline to the insects' water, which inactivates the self-limiting gene, allowing larvae to grow to adulthood. Then they sort and release adult male mosquitoes, which mate with wild females.

 Oxitec mosquito larvae glow red, while wild-type larvae do not.OXITECBecause there is not enough tetracycline in the environment to shut down the self-limiting gene, the progeny of GM-wildtype matings die young. Oxitec scientists determine how many males have mated with wild females by monitoring the presence of the fluorescent reporter in larvae they collect in simple traps and then adjust how many GM male insects they release.

The Florida Keys Mosquito Control District spends about $1.1 million per year on monitoring populations and deploying conventional insecticides to reduce *A. aegypti* numbers by half. The Florida Department of Health has recorded multiple locally acquired cases of both dengue and Zika virus in recent years, making the state a prime target for mosquito population reduction. Officials from the Florida Keys Mosquito Control District have already partnered with Oxitec to plan a pilot release, but cannot proceed without regulatory approval.

In field trials in the Cayman Islands, Panama, and Brazil, the release of Oxitec male mosquitoes has resulted in a greater than 90 percent reduction in *A. aegypti* populations. The company has also seen positive results beyond their pilot trials. A collaboration with officials in Piracicaba, Brazil, has led to the successful treatment of a neighborhood of 5,000 residents that is in the process of being expanded to cover an area that houses 300,000 people. A new facility near Piracicaba can produce 60 million GM male mosquitoes per week and serve a human population of 3 million.

"This is not a new technology," says Nimmo. "We've been deploying this in the field for seven years."

Tags

Zika virus, Oxitec, mosquitoes, infectious disease, GMO, gm animals, genetics & genomics, genetic engineering and dengue virus

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Comments

John Norris MD
Posts: 1

October 13, 2017

Shortly after the close of the FDA public comment period, practicing physicians in the Key Haven, Florida area petitioned for safety data related to these Genetically Modified (GM) Mosquitoes. [1]

These GM insects are programmed to require tetracycline as a maturation factor. If they do not receive the antibiotic in sufficient dosage to penetrate every cell and neutralize the implanted lethal gene, the insects die in early larval stage. If they receive a sufficient dosage, they will live and reproduce. [2]. In February of 2015, Genewatch UK published that a GM insect factory might be an antibiotic resistant bacteria factory. [3]. We also

felt the protocoled use of pans containing water, larva and antibiotic risked promoting resistant bacteria colonization of the GM insects.

The World Health Organization (WHO) estimates 700,000 people die each year from antibiotic resistant bacterial infections. Community meetings were held where the answer to whether resistant bacteria were present and antibiotic sensitivities were never disclosed. 14,700,000 GM insects would be released over 22 months on two populated island streets without regard to immunocompetence of inhabitants. Petitioners opposed release without bacterial resistance data on the adult, to-be-released GM insects and that data being factored into any possible release.

Barry Kreiswirth, PhD at PHRI/Rutgers University, offered his lab to genetically characterize resistance among the isolated microbes from the insect. Having a resistance genotype may provide an opportunity to track these changes among human isolates collected from both the test and control areas. In addition, one could also evaluate nasal swabs from volunteers from both test and control areas to observe changes in resistance among carriage strains. Tracking antibiogram data for resistance changes pre- and post-release also was discussed.

In 2009 and 2010, our community was sensitized to mosquito-borne illnesses by a Dengue outbreak. We appreciate the proposed benefit of this technology. We question the use of an antibiotic while neglecting that uses bacterial impact. Alexander Fleming called the misuser of antibiotics the "the ignorant man" in his 1945 Nobel Prize speech. [4] It is our opinion this data is required to make a risk benefit analysis of threat from bacterial resistance vs threat of mosquito-borne illnesses in the use of antibiotic-dependent, GM insects.

1. https://www.facebook.com/JohnWNorrisMD/posts/1000115220104948:0
2. Curtis Z, Matzen K, Neira Oviedo M, et al. Assessment of the Impact of Potential Tetracycline Exposure on the Phenotype of Aedes aegypti OX513A: Implications for Field Use. Benedict MQ, ed. PLoS Neglected Tropical Diseases. 2015;9(8):e0003999. doi:10.1371/journal.pntd.0003999.
3. Genetically Modified Insect Factories: A New Source of Superbugs? [Internet]. GeneWatch UK; 2015 Feb [Cited 2017 May 15]. Available fromhttp://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Antibiotic_GWbrief_fin.pdf
4. https://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-lecture.pdf

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